COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

Fifteenth report

WASHINGTON, DC

Updated: 2 June 2021

INDEX

Official reports on pharmacovigilance programs

CANADA

- As of 21 May 2021, 20,328,984 doses of COVID-19 vaccines of Pfizer-BioNTech, Moderna, AstraZeneca, and Covishield (AstraZeneca manufactured by the Serum Institute of India) had been administered.
- A total of 5,989 individual reports of one or more adverse events (0.029% of doses administered) were received. Of these, 1,126 were considered serious events (0.006% of doses administered), with anaphylaxis being the most frequently reported.
- Of total reports, the Pfizer-BioNTech vaccine accounted for 2,570 non-serious events and 736 serious events. For the Moderna vaccine, there were 1,782 reports of non-serious events and 133 of serious events; for the Covishield/AstraZeneca vaccine, there were 503 reports of non-serious events and 214 of serious events.
- A total of 16,582 AEFI were reported (including 5,989 reports of one or more events), of which the majority were for non-serious adverse events, such as injection-site reactions, paresthesia, pruritus, hives, headache, hypoesthesia, and nausea. A total of 69 cases of anaphylaxis were reported (59 for the Pfizer-BioNTech vaccine and 10 for the Moderna vaccine).
- As of 21 May, 54% of vaccine doses administered were to women and 46% to men. The majority of adverse events reported were among women (82% of total doses administered).
- As of the same date, there were 33 reports of thrombosis with thrombocytopenia syndrome (TTS) following vaccination with Covishield/AstraZeneca. Symptoms occurred between 3 and 30 days after vaccination; 13 were in women (ages 40 to 72), 19 were in men (ages 34 to 73), and in one case the sex of the person was not identified.
- A total of 76 reported cases of adverse events resulted in post-vaccination deaths. Following a medical review, it was determined that 25 of these deaths were not linked to administration of the COVID-19 vaccine, while 42 are under investigation; four were potentially attributable to vaccination (TTS cases), and the cause of death in five cases could not be determined due to insufficient information.

Source: https://health-infobase.canada.ca/covid-19/vaccine-safety/

SPAIN

- As of 25 April 2021, a total of 14,290,507 doses of COVID-19 vaccines had been administered to 10,425,631 individuals. The Comirnaty vaccine accounted for 70% of doses administered, Vaxzevria (formerly the AstraZeneca COVID-19 vaccine) for 24%, and Moderna for 6%, while less than one percent were for the Janssen vaccine.
- As of the same date, 17,297 AEFI had been reported. The most frequently reported events were fever, pain at the injection site, headache, dizziness, myalgia, and arthralgia.
- Of total adverse events reported, 3,171 were considered serious, of which 1,734 were associated with the Comirnaty vaccine, 237 with the Moderna vaccine, and 1,186 with the Vaxzevria vaccine.
- With regard to the thrombosis with thrombocytopenia syndrome (TTS), as of 25 April, 11 probable or confirmed cases had been reported. Most of these were in unusual locations (cerebral venous sinus thrombosis and mesenteric thrombosis); three of the patients subsequently died. With these data, the estimated notification rate is five cases per million doses of vaccine administered, ranging from 13 cases per million doses in people ages 30 to 39, to one case per million doses in people age 60 and above.

Source: https://www.aemps.gob.es/laAEMPS/docs/informe-farmacovigilancia-mayo-2021.pdf?x74586

ITALY

- From 27 December 2020 to 26 April 2021, a total of 18,148,394 doses of COVID-19 vaccines had been administered – 70.9% of Comirnaty, 22% of Vaxzevria, 7% of Moderna, and 0.1% of the Janssen vaccine.
- A total of 56,110 adverse events were reported, equivalent to 309 per 100,000 doses administered; of these, the majority (75%) were associated with the Comirnaty vaccine, followed by Vaxzevria (22%) and Moderna (3%). No AEFI were reported for the Janssen vaccine.
- Serious events accounted for 8.6% of all adverse events reported, with 27 serious events per 100,000 doses administered (24 per 100,000 doses administered for the Comirnaty vaccine; 18 for the Moderna vaccine, and 39 for the Vaxzevria vaccine).
- A total of 223 events resulting in death were reported, of which 141 occurred after the first dose and 59 after the second dose; for 23 of these events, the reports contained insufficient

data to conduct an evaluation. An assessment determined that in 56% of these deaths there was no correlation with vaccination; in 39%, a possible correlation was undetermined; and 3% were deemed unclassifiable. Only three reports (2% of total deaths) were correlated with the administration of the first dose of Vaxzevria vaccine; these involved TTS cases.

Source: https://www.aifa.gov.it/documents/20142/1315190/Rapporto_sorveglianza_vaccini_COVID-19_4_EN.pdf

MEXICO

- As of 29 May 2021, 29,861,331 doses of the Pfizer-BioNTech, AstraZeneca, CanSino, Sinovac, and Sputnik V vaccines had been administered.
- A total of 19,984 cases of adverse events following immunization (AEFI) were reported (0.07% of doses administered), of which 15,625 were associated with the Pfizer-BioNTech vaccine, 1,925 with the AstraZeneca vaccine, 1,007 with Sinovac, 359 with Sputnik V, and 1,049 with the CanSino vaccine.
- There were 401 reports of serious events, representing 2.0% of total events reported. Of these serious events, 174 occurred with the Pfizer-BioNTech vaccine, 88 with the AstraZeneca vaccine, 73 with Sinovac, 17 with Sputnik V, and 46 with the CanSino vaccine; 225 occurred in women and 176 in men.

Source: https://www.gob.mx/salud/acciones-y-programas/versiones-estenograficas-conferencia-de-prensa

UNITED KINGDOM

- As of 19 May 2021, in the United Kingdom, an estimated 12.7 million first doses of the Pfizer-BioNTech vaccine, 24.2 million first doses of the Oxford/AstraZeneca vaccine, and 0.3 million doses of the Moderna vaccine had been administered, while approximately 10.5 second doses of the Pfizer-BioNTech vaccine and 10.7 million second doses of the Oxford/AstraZeneca vaccine had been administered.
- As of the same date, there were 61,553 yellow cards reports for the Pfizer-BioNTech vaccine, 182,751 for the Oxford/AstraZeneca vaccine, and 1,972 for the Moderna vaccine, while 694 did not specify the vaccine manufacturer. For the first two vaccines, the reporting rate was approximately 3 to 7 cards per 1,000 doses administered. To be clear, yellow card data cannot

be used to draw any conclusions on the rate of adverse events, or to compare the safety profile of different vaccines, since more information is needed to do so.

- For all vaccines, the vast majority of reports were related to injection-site reactions (arm pain) or to general symptoms such as headache, chills, fatigue, nausea, fever, weakness, muscle pain, tachycardia, or flu-like symptoms. These events usually occur close to the time of vaccination and are not associated with more-serious or longer-lasting events.
- The UK Medicines and Healthcare Products Regulatory Agency (MHRA) received 317 spontaneous reports of anaphylaxis (severe allergic reactions) associated with the Pfizer-BioNTech vaccine.
- There were 674 spontaneous reports of adverse events involving anaphylaxis or anaphylactic reactions for the AstraZeneca vaccine. Although these events are very rare, the product information has been updated to reflect the fact that cases of anaphylaxis have been reported after administration of the vaccine.
- Regarding events involving Bell's palsy (facial palsy), the MHRA continues to review reports of facial paralysis and to compare them against cases that would be expected to occur randomly in the general population (baseline rate). The number of cases reported, to date, is similar to the baseline rate, and there is no indication that this will increase with vaccination. These events continue to be monitored.
- With regard to thromboembolic events with thrombocytopenia, the MHRA received 332 yellow card reports following vaccination with the AstraZeneca vaccine (180 in women and 151 in men), with 58 deaths, a case fatality rate of 17%. There were 17 reported cases of deaths following administration of the second dose of the vaccine. The event has a reporting frequency of 13.0 per million doses administered, with the incidence in young adults appearing to be higher than in the older age group. However, based on ongoing data, the Agency continues to recommend that, for the majority of the population, the benefits of the vaccine outweigh the risks.
- There have been seven reported cases of capillary leak syndrome (a condition in which blood leaks from small blood vessels to the body) associated with the AstraZeneca vaccine, out of more than 34 million doses of the vaccine administered. Current evidence does not indicate a causal relationship between this syndrome and the vaccine.

Yellow cards are a mechanism by which anyone can voluntarily report suspected adverse reactions or side effects associated with the vaccine. It should be emphasized that a yellow card report does not necessarily mean that the vaccine caused the reaction or the event.

Link: https://www.gov.uk/government/publications/coronavirus-covid-19-vaccine-adverse-reactions/coronavirus-vaccine-summary-of-yellow-card-reporting

Updates

Emergency use listing: Sinovac's COVID-19 vaccine

The CoronaVac COVID-19 vaccine, developed by China's Sinovac Laboratory, was added to the emergency use listing of vaccines (EUL) of the World Health Organization (WHO) on 1 June 2021, with the following general description:

Product characteristics

Name	COVID-19 vaccine (vero cell), inactivated
Commercial name	CoronaVac
WHO date of recommendation	1 June 2021
Platform/Type of vaccine	Inactivated COVID-19 vaccine (vero cell)
Manufacturer	Sinovac Biotech: Tianfu Street, Daxing Biomedicine Industrial Base of Zhongguancun Science Park, Daxing District, Beijing, P.R. China
Pharmaceutical form	Suspension for injection
Presentation	Prefilled syringe and 1-dose vial
Diluent	N/A
Dose/Route of administration	0.5 mL intramuscular
Storage temperature/Shelf life	+2° to +8°C for 12 months
Open vial/In use	Once the syringe or vial is opened, use immediately.

Source: https://extranet.who.int/pqweb/vaccines/who-recommendation-sinovac-covid-19-vaccine-vero-cell-inactivated-coronavac

Preliminary results on the benefits of combining different COVID-19 vaccines

Researchers involved in different clinical studies have indicated that combining COVID-19 vaccines from different platforms could trigger a more robust immune response, compared to administering two doses of the same vaccine; this would also simplify immunization efforts in countries facing fluctuating supplies of the various vaccines.

The Spanish clinical trial known as CombivacS, led by the Carlos III Health Institute, began in Madrid in April 2021, with 663 participants under the age of 60 who had received a first dose of the Oxford/AstraZeneca vaccine. Two-thirds of the participants were selected at random to receive the

Pfizer-BioNTech mRNA vaccine at least eight weeks after receiving their first dose, while the remaining 232 participants were assigned to the control group, which has not yet received a second, booster dose.

Preliminary results from the trial indicate that those who had received the second dose developed much higher antibody levels than the control group, with laboratory tests showing the presence of neutralizing antibodies against SARS-CoV-2. The increase in antibody titers appears to be greater than in most people who receive two doses of the Oxford/AstraZeneca vaccine, according to data from previous trials. In terms of reactogenicity, the vaccinated group maintained a profile similar to that of the Comirnaty vaccine in homologous vaccination regimens. Participants in the CombivacS trial control group experienced no change in antibody levels.

A similar study conducted in the UK, known as Com-COV, which analyzed a combination of the same two vaccines, found that in people who received a different vaccine for the second dose, there was an increase in symptoms such as fever, between 24 and 48 hours after vaccination, compared to people who received two doses of the same vaccine. The primary immunological result of this Com-VOC trial is expected to be available in June 2021.

Sources:

Mix-and-match COVID vaccines trigger potent immune response. Nature 593, 491 (2021) doi: https://doi.org/10.1038/d41586-021-01359-3

Heterologous prime-boost COVID-19 vaccination: initial reactogenicity data. The Lancet. May 12, 2021 doi: https://doi.org/10.1016/S0140-6736(21)01115-6

Report of the Butantan Institute: Impact of mass vaccination in the municipality of Serrana (preliminary results not yet peer reviewed)

During the most recent four months of this year, researchers at the Butantan Institute measured the effects of large-scale immunization in the city of Serrana, in the interior of the state of São Paulo. The city, with 45,000 inhabitants, was chosen for mass vaccination because it had a high infection rate. In April 2021, once vaccinations had begun, Serrana already experienced a significant drop in the incidence of COVID-19. From 699 cases in March, the number of cases dropped to 251. In the same period, deaths went from 20 to 6. Results also showed that vaccination protected both adults who received the two doses of the vaccine and, by extension, unvaccinated children and adolescents under the age of 18.

According to the researchers, the pandemic was brought under control after three of four groups received the second dose, that is, about 75% of the population. According to the Butantan Institute,

shortly after the vaccinations ended, the number of deaths in Serrana decreased by 95%, while the number of symptomatic cases of COVID-19 declined by 80%, and the number of hospitalizations dropped by approximately 86%.

Source: https://butantan.gov.br/noticias/immunization-of-serrana%C2%B4s-population-with-butantan%C2%B4s-vaccine-has-a-high-decrease-of-80-cases-and-95-in-deaths-by-covid-19

Clarifications/Conclusions regarding events presented in previous communications

Information from WHO's GACVS subcommittee regarding reports of cases of myocarditis following administration of mRNA-based COVID-19 vaccines

On 26 May 2021, the COVID-19 subcommittee of the Global Advisory Committee on Vaccine Safety (GACVS) published information on the WHO website related to reported cases of myocarditis following administration of mRNA-based COVID-19 vaccines.

They indicated that on 17 May 2021, the CDC's COVID-19 Technical Work Group, of the Advisory Committee on Immunization Practices (ACIP), concluded that few cases of myocarditis had been reported to date. These cases appear to occur predominantly in adolescents and young adults, and more often in young men than in young women, most often within four days of receiving the second dose of the vaccine. Most of the cases were mild and continue to be monitored.

The GACVS subcommittee noted that most of the information received so far is based on passive and spontaneous reports, and that more rigorous studies using alternative data sources and stronger study designs, including comparison of vaccinated and unvaccinated populations, are needed in order to assess a possible causal association between the event and the vaccine. Some countries, such as Israel, the United Kingdom, and the United States, will be initiating such studies. The GACVS subcommittee emphasized that it was important to have a harmonized case definition, and that the Brighton Collaboration had recently developed a draft case definition of myocarditis.

While recognizing the clear benefits of mRNA vaccines in reducing deaths and hospitalizations due to infection by the COVID-19 virus, the subcommittee is encouraging health professionals to report all myocarditis and other adverse events observed with these and other vaccines. WHO's COVID-19 Vaccine Safety Surveillance Manual provides guidance to countries on monitoring safety and sharing data regarding adverse events associated with new COVID-19 vaccines.

Source: https://www.who.int/news/item/26-05-2021-gacvs-myocarditis-reported-with-covid-19-mrna-vaccines

Other related updates

The Spanish Agency for Medicines and Medical Devices updates materials on the safety of COVID-19 vaccines

The Spanish Agency for Medicines and Medical Devices, in its pharmacovigilance report on vaccines against COVID -19, published on 11 May 2021, indicated that after reviewing available safety data, the following conclusions could be drawn:

- Comirnaty (Pfizer-BioNTech) vaccine: Skin rash and pruritus (infrequent) and hives (rare) have been included as possible adverse reactions. The possible appearance of localized inflammation after vaccination in people who had previously received facial filler injections was also added as a possible adverse reaction.
- Vaxzevria (AstraZeneca) vaccine: Information on the occurrence of thrombosis with thrombocytopenia syndrome (TTS) in unusual locations, such as cerebral venous sinuses and in splenic veins, was included as a possible adverse reaction to the vaccine. The possible occurrence of isolated thrombocytopenia was also cited. In addition, the Agency noted that a possible association between the vaccine and cases of capillary leak syndrome is being studied, after a number of isolated cases had been reported.
- Janssen COVID-19 vaccine: Information regarding the occurrence of thrombosis with thrombocytopenia in unusual locations, such as cerebral venous sinuses and in splenic veins, was included as a possible adverse reaction to this vaccine. Occurrence of this condition is very rare.

Source: https://www.aemps.gob.es/laAEMPS/docs/informe-farmacovigilancia-mayo-2021.pdf?x74586

The European Medicines Agency authorizes the Comirnaty COVID-19 vaccine in children ages 12 to 15

On 28 May 2021, the Committee for Medicinal Products for Human Use, of the European Medicines Agency (EMA/CHMP), recommended granting an extension of indication for the Pfizer COVID-19 vaccine Comirnaty to include use in children ages 12 to 15. This vaccine had initially been approved for use in adults and in adolescents age 16 and older. The vaccination schedule for children ages 12 to 15 will be the same: two injections in the muscles of the upper arm, given three weeks apart.

The effects of the Comirnaty vaccine in children were studied in 2,260 children ages 12 to 15; the trial showed that the immune response to the Comirnaty vaccine in this group was comparable to the

immune response in the 16 to 25 age group (as measured by the level of antibodies against SARS-CoV-2). The efficacy of the Comirnaty vaccine was assessed in nearly 2,000 children ages 12 to 15; of the 1,005 children who received the vaccine, none developed COVID-19, compared to 16 of the 978 children in the placebo group who contracted the disease. Thus, in this study the vaccine was 100% effective in preventing COVID-19 (although the actual rate could be between 75% and 100%).

Source: https://www.ema.europa.eu/en/news/first-covid-19-vaccine-approved-children-aged-12-15-eu

FDA authorizes longer time for refrigerator storage of thawed Pfizer-BioNTech COVID-19 vaccine prior to dilution

The U.S. Food and Drug Administration (FDA) reported that it had authorized an extension of the time period for refrigerator storage of thawed Pfizer-BioNTech COVID-19 vaccine prior to dilution, based on a review of data submitted by Pfizer demonstrating that undiluted, thawed vials of its COVID-19 vaccine are stable at refrigerator temperatures of 2°C to 8°C (35°F to 46°F) for up to one month.

Previously, the FDA had authorized thawed, undiluted vials of Pfizer-BioNTech's COVID-19 vaccine to be stored between 2°C and 8°C (35°F to 46°F) for up to five days.

Source: https://www.fda.gov/news-events/press-announcements/fda-brief-fda-authorizes-longer-time-refrigerator-storage-thawed-pfizer-biontech-covid-19-vaccine

Naming SARS-CoV-2 variants

The systems used by GISAID, Nextstrain, and Pango to name and track SARS-CoV-2 genetic lineages will continue to be used by scientists and in scientific research. In attempts to aid public discourse on COVID-19 variants, WHO convened a group of scientists from the WHO Working Group on Virus Evolution, the WHO COVID-19 Reference Laboratory Network, representatives from GISAID, Nextstrain, and Pango, and other experts in microbial virological nomenclature and communication from various countries and agencies. They were tasked with devising easy-to-pronounce and non-stigmatizing labels for variants of concern (VOC) and variants of interest (VOI). The group of experts convened by WHO recommended the use of letters of the Greek alphabet – alpha, beta, gamma, etc. – which will be easier and more practical to discuss for non-scientific audiences.

SARS-CoV-2 variants of concern and variants of interest, updated 31 May 2021

Variants of Concern (VOC): SARS-CoV-2 variant that meets the definition of a VOI and, through a comparative assessment, has been shown to be associated with one or more of the following changes in degree of importance to global public health:

- Increased transmissibility or detrimental change in the epidemiology of COVID-19; or

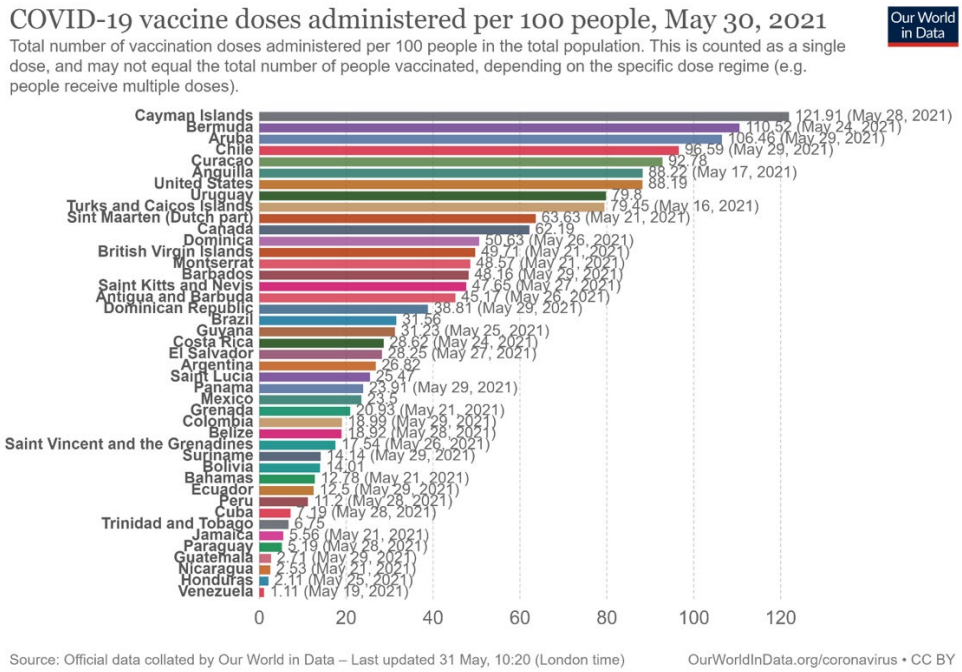
- Increased virulence or change in the clinical presentation of the disease; or
- Decreased effectiveness of social and public health measures, or of available diagnostics, vaccines, and therapies.

Below is a summary of VOC data identified to date:

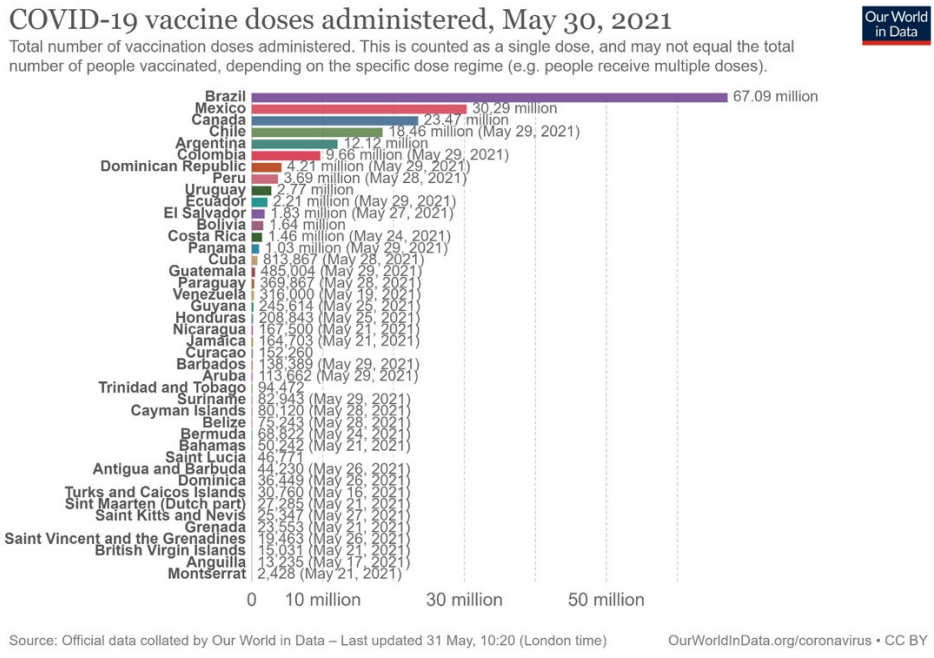
Name assigned by WHO	Pango lineage	GISAID clade/lineage	Nextstrain clade	First documented samples	Date of designation
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I/S:501Y.V1	United Kingdom, Sep 2020	18 Dec 2020
Beta	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May 2020	18 Dec 2020
Gamma	P.1	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov 2020	11 Jan 2021
Delta	B.1.617.2	G/452R.V3	21A/S:478K	India, Oct 2020	VOI: 4 Apr 2021 VOC: 11 May 2021

Use of COVID-19 vaccines in the Region of the Americas as of 30 May 2021

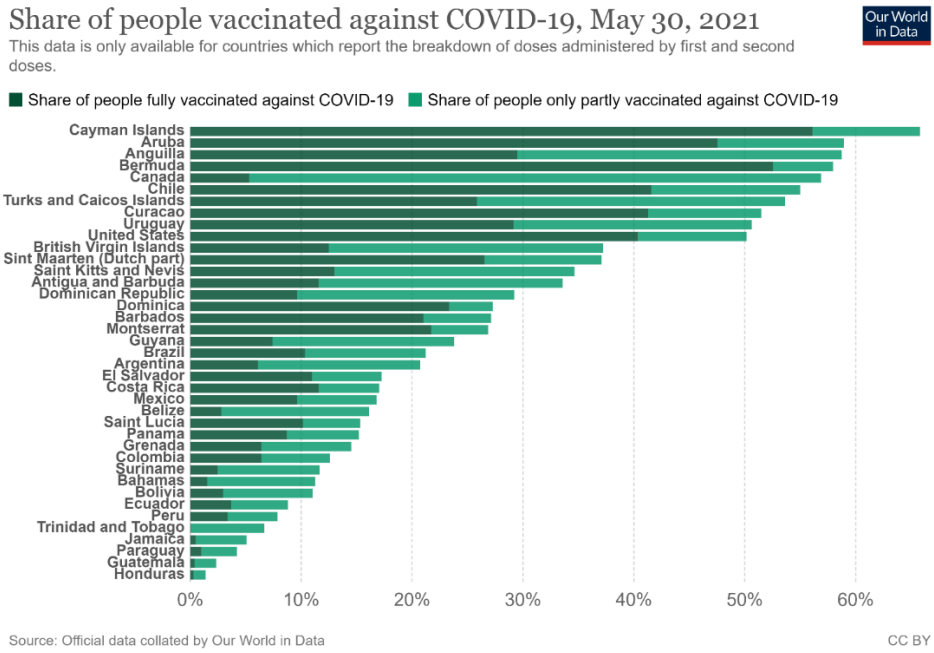
Following are consolidated data on doses administered per 100 people in the total population, by country, total doses administered, and percentage of the population partially or totally vaccinated as of 30 May 2021. The count represents single doses, and may not match the number of people vaccinated, depending on the specific dosing regimen (since some people receive multiple doses). In the second figure, the United States, with 294.93 million doses administered as of 30 May 2021, is not included.



Source: Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations



Source: Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations



Source: Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations

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